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Biochemistry of Chronic Obstructive Lung Disease.

The objective of this proposal is to determine the roles in tissue proteolysis of -1 proteinase inhibitor (-1-antitrypsin), granulocytic elastase and other proteases from granulocytes and macrophages.

In particular, the investigators wish to determine what structural differences account for the inability of -1-PI type ZZ (and also type MZ) individuals to secrete sufficient amounts of inhibitor to combat proteolysis. They would also like to know the mechanism by which the inhibitor normally functions in order to possibly develop synthetic inhibitors. Finally, they would like to determine how the granulocytic and macrophage proteases function, in order to, again possibly, develop better synthetic inhibitors to these enzymes.

In this respect the researchers hope to extend studies of this system to an investigation of the development of emphysema in individuals with normal -1 PI levels. Thus, in individuals who inhale large quantities of particulate matter (i.e., cigarette smoke), are macrophage proteases being released in quantities large enough to overwhelm the normal defense mechanism or does the macrophage actually produce proteases which can digest lung tissue but which are not inhibitable by -1-PI?

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